

EXHIBIT A

Education:

1976-81 B. Sc. and M. Sc. Université de Sherbrooke, Canada.
1981-86 Ph. D. Molecular Biophysics and Biochemistry. Yale University.
1986-88 PDF. Mount Sinai Hospital Research Institute, Toronto.

Positions:

1988- Assistant professor/Associate professor/Full professor. Dép. de
microbiologie, Faculté de médecine, Université de Sherbrooke.
1999- Head. Dép. de Microbiologie et d'Infectiologie, Sherbrooke.
2000-05 President, Telogene Inc., Sherbrooke. Canada.

Awards and Grants:

1989-94 Research Scholar, MRC
1994-01 Research Scholar (Junior II and Senior) FRSQ
2001-08 Canada Research Chair in Functional Genomics
2004- Currently supported by grants from CIHR, NCIC, CRC and Genome-
Canada
2007- Fellow of the Canadian Academy of Health Sciences

Professional service:

1993-98 Member and scientific officer BMA panel, MRC
1999 Member, Metastasis and Tumor Biology NCIC
2000 Member for CIHR Scientific Director Interview Committee
2001 Member, committee CIHR Investigators
2000-08 Member, *Molecular and Cellular Biology* Editorial Board
2002-07 Member, *The Journal of Biological Chemistry* Editorial Board
2005, 07 Panel member and reviewer, Sixth Framework Programme on Life
Sciences, Genomics and Biotechnology for Health, European Commission

Publications (since 2003)

38. Chabot, B., LeBel, C., Hutchison, S., Nasim, F. H. and Simard, M. J. (2003) HnRNP A/B proteins and the control the alternative splicing of the mammalian hnRNP A1 pre-mRNA. **Progress in Molecular and Subcellular Biology. Regulation of alternative splicing.** Springer-Verlag GmbH & Co. Heidelberg. Vol 31, pp. 59-88.
39. Naud, J.-F., Gagnon, F., Chabot, B., Wellinger, R., Lavigne, P. (2003). Improving the thermodynamic stability of the leucine zipper of max increases the stability of its b-HLH-LZ:E-box complex. **J. Mol. Biol.** 326, 1577-1595.

40. Gagné, J.-P., Hunter, J., Labrecque, B., Chabot, B. and Poirier, G. G. (2003). A proteomic approach to the identification of heterogeneous nuclear ribonucleo-proteins as a family of poly(ADP-ribose)-binding proteins. **Biochem. J.** 371:331-340.
41. Patry, C., Bouchard, L., Labrecque, P., Gendron, D. Lemieux, B., Toutant, J., Lapointe, E., Wellinger, R. and Chabot, B. (2003). siRNA-mediated reduction in hnRNP A1/A2 proteins induces apoptosis in human cancer cells but not in normal mortal cell lines. **Cancer Res.** 63, 7679-7688.
42. Villemaine, J., Dion, I., Abou Elela, S., and Chabot, B. (2003) Reprogramming alternative pre-messenger RNA splicing through the use of protein-binding antisense oligonucleotides. **J. Biol. Chem.** 278: 50031-50039
43. Bériault, V., Clément, J. F., LeBel, C., Yong, X., Chabot, B., Cohen, E. A., Cochrane, A. W., Rigby, W. F. C., and Mouland, A. J. (2004). A late role for the association of hnRNP A2 with the HIV-1 hnRNP A2 response elements in genomic RNA, Gag and Vpr localization. **J. Biol. Chem.** 279: 44141-44153.
44. Patry, C, Lemieux, B., Wellinger, R. and Chabot, B. (2004). Targeting hnRNP A1 and A2 by RNA interference promotes cell death in transformed but not normal mouse cell lines. **Mol. Cancer Ther.** 3(10):1193-1199.
45. Garneau, D, Revil, T, Fisette, J.-F., Chabot B. (2005). hnRNP F/H proteins control the alternative splicing of the apoptotic mediator Bcl-x. **J. Biol. Chem.** 280:22641-22650.
46. Naud, J.-F., McDuff, F.-O., Sauvé, S., Montagne, M., Webb, B. A., Smith, S. P., Chabot, B. and Lavigne, P. (2005). Structural and thermodynamical characterization of the complete p21 gene product of Max. **Biochemistry** 44:12746-12758.
47. Gendron, D., Carriero, S., Garneau, D., Villemaine, J., Klinck, R., Abou Elela, S. Damha, M. J. and Chabot, B. (2006). Modulation of 5' splice site selection using tailed oligonucleotides carrying splicing signals. **BMC Biotechnology** 6:5
48. Martinez-Contreras, R., Fisette, J.-F., Nasim, F. H., Madden, R., Cordeau, M. and Chabot, B. (2006). Intronic Binding Sites for hnRNP A/B and hnRNP F/H Proteins Stimulate Pre-mRNA Splicing. **PLoS Biol.** 4:172-185.
49. Revil, T., Shkreta, L., and Chabot, B. (2006). [Pre-mRNA alternative splicing in cancer: functional impact, molecular mechanisms and therapeutic perspectives] **Bull. Cancer** 93(9):909-19. In French.
50. Zhuo, D., Madden, R., Abou Elela, S. and Chabot B. (2007). Modern origin of numerous alternatively spliced human introns from tandem arrays. **Proc. Natl. Acad. Sci. U.S.A.** 104: 882-886.
51. Jérónimo, C., Forget, D., Bouchard, A., Chua, G., Poitras, C., Li, Q., Thérien, C., Bergeron, D., Bourassa, S., Greenblatt, J., Chabot, B., Poirier, G., Price, D., Hugues, T. R., Blanchette, M., Coulombe, B. (2007) Protein complexes formed by the mammalian transcription machinery include a 7SK/U6 snRNP with RNA capping activity. **Molecular Cell.** 27: 262-274.
52. Paradis, C., Cloutier, P., Toutant, J., Klarskov, K., and Chabot B. (2007) hnRNP I/PTB can antagonize the splicing repressor activity of SRp30c. **RNA** 13:1287-1300.

53. Revil, T., Toutant, J., Shkreta, L., Garneau, D., Cloutier, P. and Chabot, B. (2007). Protein kinase C-dependent control of Bcl-x alternative splicing. **Mol. Cell. Biol.** 27: 8431-8441.
54. Martinez-Contreras, R., Fisette, J. F., Cloutier, P., Revil, T., Shkreta L. and Chabot, B. (2007). hnRNP proteins and splicing control. **Alternative splicing in the postgenomic era**. Landes Biosciences Series. B. Blencowe and B. Graveley, editors. pp. 123-147.
55. Klinck, R., Bramard, A., Inkel, L., Dufresne-Martin, G., Gervais-Bird, J., Madden, R., Paquet, E., Venables, J. P., Prinos, P., Jilaveanu-Pelms, M., Rancourt, C., Wellinger, R., Chabot, B., and Abou Elela, S. (2008). Multiple alternative splicing markers in ovarian cancer. **Cancer Res.** 68: 657-663.
56. Parenteau, J., Durand, M., Véronneau, S., Lacombe, A.-A., Morin, G., Guérin, V., Gervais-Bird, J., Koh, C.-S., Brunelle, D., Cecez, B., Wellinger, R., Chabot, B., and Abou Elela, S. (2008). Systematic deletion of many yeast introns reveals a minority of genes that require splicing for function. **Mol. Biol. Cell.** 19: 1932-1941.
57. Shkreta, L., Froelich, U., Paquet, E. R., Toutant, J., Abou Elela, S. and Chabot, B. (2008). Impact of anticancer drugs on the alternative splicing of Bcl-x and other apoptotic genes. **Mol. Cancer Ther.** (in press).

circumscribes the targeted region. PCR amplifications (2 min at 50°C, 10 min at 95°C; 40 cycles: 15 sec at 95°C, 1 min at 60°C) were done in 25 µl reactions using 50 ng of template cDNA, 900 nM of each forward and reverse primers and 250 nM of TaqMan probe (See Table 3 of Exhibit C). Quantitative analysis was done with RQ Study software provided by Applied BioSystem. A endogenous internal control (GAPDH) was also concomitantly reverse transcribed and amplified in all samples for data normalization .

b. SyBrGreen qPCR approach (for KITLG gene)

Briefly,reverse transcription was performed on 250 ng of cell total RNA with Transcriptor, random primer p(dN)6 and dNTPs (Roche Diagnostics, Laval, QC, Canada) and porcine RNAGuard (Amersham) as recommended by the manufacturer. All real-time PCR reactions were done on a 7500 ABI apparatus (Applied Biosystems, Foster City, CA) with Power SYBR Green master mix (Applied Biosystems Canada, Streetsville, ON, Canada). PCR amplifications (10 min at 95°C; 50 cycles: 15 sec at 95°C, 30 sec at 60°C, 31 sec at 72°C; melting curve: 15 sec at 95°C, 60 sec at 60°C; 1°C/min temperature gradient, 15 sec at 95°C) were performed in 10 ul reactions using 10 ng of template cDNA and 200 nM of each forward and reverse primer (see Table 2 of Exhibit C). Normalization factor was calculated using geometric mean mRNA level of PSMC4 and RPL13A.

Results

Table. qPCR value relative to LF (lipofectamine only) as calibrant set at 1

GENE	Oligonucleotides	L mean	S mean	Ratio:L mean/S mean
DNMT3B	LF	1	1	1
	Toss	0,274	2,2995	0,119
	As	0,498	2,0115	0,247
	A1Casp8-4	0,98	0,9885	0,991
C11orf 17	LF	1	1	1
	Toss	0,3355	1,5605	0,215
	As	0,7975	1,605	0,4969
	A1Casp8-4	0,909	0,9115	0,997
BMP4	LF	1	1	1
	Toss	0,7505	1,6765	0,448
	As	0,7875	1,1215	0,702
	A1Casp8-4	1,0375	1,0595	0,979
CHEK 2	LF	1	1	1
	Toss	0,5615	1,6365	0,343
	As	0,993	1,08	0,919
	A1Casp8-4	1,0555	0,965	1,094
FGFR1	LF	1	1	1
	Toss	0,343	1,587	0,216
	As	0,4715	1,375	0,3429

	A1Casp8-4	1,05	1,0175	1,032
KITLG	LF	1	1	1
	Toss	0,4	3,14	0,127
	As	0,75	1,24	0,6051
	TOSS AllStar	0,78	1,07	0,729

L mean and S mean values are the combination of three independent experiments

As shown in the Table above, tailed oligos (TOSS) that hybridize in the alternative exon near a 5' splice site and bind to a protein moiety are more efficient at inhibiting exon inclusion than oligos with no tail (As or classical antisens oligonucleotide) or oligos with tails that do not hybridize to the targeted exon (TOSS Allstar or A1Casp84). The activity of each oligo is compared to LF (no oligo transfected; lipofectamine only; given an arbitrary value of 1). Exon inclusion was examined by monitoring the abundance of the long (exon included) and short (exon excluded) isoforms independently by quantitative real-time RT-PCR (qRT-PCR). Oligos that are more efficient at inhibiting exon inclusion decrease the long isoform and/or increase the short isoform of the mRNA, thereby overall decreasing the ratio L mean/S mean. Thus, in all cases, TOSS oligos produce a global shift in favor of the short isoform that is better than the As oligos. These result also indicate that the TOSS oligonucleotides do not act by depleting a factor (e.g., the hnRNP A1 protein) because control TOSS oligos essentially have no activity (A1Casp8-4 is a tailed oligo that hybridizes to another gene whereas TOSS AllStar has a scramble region that does not hybridize to anything known).